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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/606,632	06/26/2003	Masaya Takaoka	03260CIP/HG	4979

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EXAMINER	
ZHANG, NANCY L	
ART UNIT	**PAPER NUMBER**
1614	

DATE MAILED: 08/31/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/606,632	TAKAOKA ET AL.	
	Examiner	Art Unit	
	Nancy L. Zhang	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 March 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *6 and 22-35* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *6* is/are allowed.

6)☒ Claim(s) *22-35* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *2 sheets*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicant's amendment filed on March 15, 2006 has been received. In the filed amendment, the applicant added new claims 22-35.

Applicant's affidavits of drug reports as evidence for known insulin sensitizers filed on March 15, 2006 has been received and has been taken into consideration.

Because of the cancellation of previous broad claims, the addition of more specified claims along with the applicant's submitted affidavits of drug reports, the previous enablement rejection under *35 USC § 112* is withdrawn.

Claims 1-5 and 7-21 are cancelled.

Claims 6 and the newly added claims 22-35 are presented for examination.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to

consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 22-35 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hosakawa (PTO 1449) and Robl (US PGPub: 20020013334, pub. Date: Jan. 31, 2002) in view of Cropp (US Pat: 6,245,787, issue date: Jun. 12, 2001), further in view of (US Pat: 6,245,787, issue date: Jun. 12, 2001), Mizukami (PTO 892, item U), Fukui (PTO 892, item V), Devasthale (PTO 892, item W) and Kitahara (US PGPub: 20030073729, pub. Date: Apr. 17, 2003).

Claims 22-23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hosokawa et al., "Troglitazone inhibits bicarbonate secretion in Rat and Human Duodenum". Journal of Pharmacology and Experimental Therapeutics. September 1999, page 1080-1084. (Form 1449).

Claims 22 and 23 recite a pharmaceutically composition comprising a diuretic and an insulin sensitizer in a ratio of 1:200 to 200:1 where the diuretic is amiloride and the insulin sensitizer can be a troglitazone.

Hosakawa teaches the administration of troglitazone combined with the administration of amiloride. Table 1 (page 1082) demonstrates that troglitazone (20 μM) and amiloride (100 μM) are used in the combined administration resulting in a ratio of 1:5 between troglitazone and amiloride. Hosakawa does not teach troglitazone and amiloride being combined into one pharmaceutical composition. However, it would have been obvious to one of ordinary skill in the art at the time of the claimed invention was made to make a pharmaceutical composition comprising troglitazone and amiloride

in a ratio of 1:5. The motivation to do so is provided by Hosakawa that the administration of troglitazone (an insulin sensitizer) has a propensity to cause edema (page 1080, column 1, line 7), and the administration of diuretics should safely relieve the fluid retention induced by troglitazone (page 1084, column 1, line 26) and that it is possible to continue the combined prescription of troglitazone and diuretics for the patients with edema (page 1084, column 1, line 30).

Thus, the claimed invention of claims 22 and 23 was *prima facie* obvious over the teachings of Hosakawa.

Claims 22-35 are rejected under 35 U.S.C. 103(a) as being unpatentable over Robl (US PGPub: 20020013334, pub. Date: Jan. 31, 2002) in view of Cropp (US Pat: 6,245,787, issue date: Jun. 12, 2001), further in view of (US Pat: 6,245,787, issue date: Jun. 12, 2001), Mizukami (PTO 892, item U), Fukui (PTO 892, item V), Devasthale (PTO 892, item W) and Kitahara (US PGPub: 20030073729, pub. Date: Apr. 17, 2003).

Claims 22-35 are directed to a pharmaceutical composition comprising a diuretic and an insulin sensitizer where the diuretic is amiloride and the insulin sensitizer is selected from a group consisting of troglitazone, pioglitazone, rosiglitazone, JTT-501, MCC-555, GI-262570, YM-440, KRP-297, T-174, NC-2100, BMS-298585, AZ-242 and NN-622.

Robl teaches a pharmaceutical composition comprising a HMG CoA reductase inhibitor and one or more other types of therapeutic agents including antidiabetic agents and antihypertensive agents (page 18, claim 17, lines 5-6). The antidiabetic agents can

be insulin sensitizers (page 18, paragraph [0213], line 5). The antihypertensive agents can be diuretics (page 20, paragraph [0247], line 8). Robl further discloses compounds used as antidiabetic agents can be insulin sensitizers such as troglitazone, pioglitazone, rosiglitazone, JTT-501, MCC-555, GI-262570, YM-440 (page 19, paragraph [0220], lines 5-10) and KRP-297 (page 19, paragraph [0229], line 4).

Robl does not teach the use of particular compounds of T-174, NC-2100, BMS-298585, AZ-242 and NN-622 in combination with the HMG CoA reductase inhibitor. However, Robl discloses that the antidiabetic agents that may be employed in the combination can be insulin sensitizers including PPAR γ agonists such as thiazolidinediones and PPAR α/γ dual agonists (page 18, [0213], lines 7-9). Mizukami discloses T-174 is a thiazolidinedione compound developed as an antidiabetic drug stimulating the transcription of PPARγ (page 61, line 5 of abstract); Fukui discloses NC-2100 is a PPARγ activator exhibiting potent antidiabetic effects (see title). Kitahara discloses NN-622 is a PPAR γ agonist (page 2, [0031], line 11); Devasthale discloses BMS-298585 (page 2248, line 1 of abstract) and AZ-242 (page 2248, left column, lines031-32) are PPAR α/γ dual agonists. Therefore, the compounds of T-174, NC-2100, BMS-298585, AZ-242 and NN-622 are all insulin sensitizers within the scope of Robl's disclosure.

Robl does not teach the use of amiloride as the diuretic. However, Cropp teaches that amiloride is a useful diuretics (column 3, line 12).

Robl also discloses that when a combination is administered, the compound of Robl's invention can be employed in a weight ratio to other types of therapeutic agents within the range from about 0.5:1 to about 100:1.

Therefore, it would have been obvious to one of ordinary skill in the art at the time of the claimed invention was made to make a pharmaceutical composition according to Robl using amiloride as the diuretic and one of the above listed known insulin sensitizers in combination with the inhibitor of Robl's invention. The motivation to do so is to make and use Robl's invention. If weight ratios in the composition are 1:1 between amiloride and Robl's inhibitor and 1:1 between the insulin sensitizer and Robl's inhibitor, the resulting pharmaceutical composition would comprise amiloride and an insulin sensitizer with a weight ratio of 1:1 between amiloride and the insulin sensitizer. The resulting weight ratio falls into the range of 1:200 to 200:1. Therefore the resulting pharmaceutical composition meets all the limitations as defined in claims 22-35 of the instant application.

Thus, the claimed invention of claims 22-35 was *prima facie* obvious over the combined teachings of the prior art.

Conclusion

Claims 22-35 are not allowed.

Claim 6 is in condition for allowance.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nancy L. Zhang whose telephone number is (571)-272-8270. The examiner can normally be reached on Mon.- Fri. 8:30am - 5:00pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached on (571)-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

NLZ 8/24/06

NLZ

Ardin H. Marschel 8/27/06

ARDIN H. MARSCHEL
SUPERVISORY PATENT EXAMINER